ORIGINAL ARTICLES

OPERATIVE RESULTS IN CATARACTS COINCIDENT WITH DINITROPHENOL THERAPY

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DISCUSSION *by M. N. Beigelman, M. D., Los Angeles; M. L. Tainter, M. D., San Francisco; W. D. Horner, M. D., San Francisco.*

IN May, 1935, our attention was first drawn to the coincidence between the ingestion of dinitrophenol and the formation of cataracts. One of us had been told by Doctor Nutting of Oakland that he had seen a case he believed to have displayed such a coincidence. About a week later there appeared in the office an obese woman who had lost sixty pounds of weight over a period of eight months, after she had taken dinitrophenol, and who had recently lost the vision of both eyes. The following week another patient was seen with the same history and clinical findings. This patient was referred by Dr. W. D. Horner for consultation. Doctors Horner, Jones and Boardman[11] were the first in the literature to draw attention to the coincidence between the ingestion of dinitrophenol and the later formation of cataracts, with the warning that the medical profession might find cataracts to be a complication of the therapy. They advised that the administration of dinitrophenol be stopped until it was shown whether or not more cases of cataract in relation with the use of the drug developed. Meanwhile, Dr. Frank Rodin[1] has reported cases in and about the San Francisco Bay region to the number of thirty-six. Since this report we have seen two more such afflicted, and undoubtedly other cases have been noted by other physicians, so that the total number is still rising. This paper describes the clinical appearance of some of these patients and the results of operations on twenty eyes operated upon for cataracts in this group.

There are several common factors in all these operative cases. The patients are all women; they have all been obese; they have taken dinitrophenol; they have all lost weight; they are all of an age, but for one case in which development of cataract as a senile phenomenon, so-called, does not take place; they all saw well before the ingestion of dinitrophenol, and before their loss of weight; none of them, since operation, have shown a fundus condition which could have been responsible for cataract formation; only one had diabetes; none gave a history of early cataract formation in their immediate family; they all complained of loss of vision within six months to a year after having stopped dinitrophenol, and two of them of that loss while still taking it. The cataracts were bilateral, sometimes one more mature than its fellow, and in several cases they were equally mature; some women still saw enough with one eye to be not entirely helpless, others were brought in with only light projection and perception in either eye; while all, with one exception, had been fat but had lost considerable weight. The rapidity of cataract formation has been astonishing. One patient with a mature cataract on one eye, and still able to walk about comfortably with the other, lost her vision entirely on the unoperated eye while under hospital observation in bed following operation, and then had this second eye operated upon.

From the clinical point of view, then, these cataracts in this reported group are of a type that have not before occurred in our operative cataract material. The study of the tables is better than any lengthy description. The main points to be noted, however, are: that most of the extractions can be done by linear extraction and in most cases a round pupil can be obtained; and that we did not attempt any intracapsular extractions due to the fact that we did not know whether or not there might be complicating factors, such as vitreous degeneration, and that many of these lenses were so intumescent, and the capsule so thin, that an intracapsular extraction would have been difficult or impossible. It is further to be noted that in two cases vitreous loss occurred—in one, a marked amount of fluid vitreous, in the other a small bead only; that in many cases the chamber was extremely shallow—small hemorrhages, coming seemingly from the wound without rupture of the same occurred in several cases; and, further, that the vision was excellent in almost all cases and no deleterious effect on the eye other than the formation of these cataracts was observed in later careful examination. The cases in the tables are partly private, and partly those operated upon on the clinic service of Stanford University Medical School. While it is a great misfortune that even a small percentage of those taking dinitrophenol have been afflicted with cataracts, it is reassuring to know that operation is fairly easy and, in cases not otherwise complicated, promises excellent vision. What the processes are that tend to such rapid cataracts in some people losing weight due to the action of ninitrophenol we do not as yet know. One of us is at present engaged in collaboration with the department of pharmacology in an attempt at solving this problem.

This investigation brings up again the problems of cataract etiology in general. A review of the literature in regard to research in cataract etiology and normal lens metabolism leaves one in great doubt as to the probable mechanism of cataract formation in cases of this kind. A great deal of work has recently been done on the investigation of the vitamin C content of the aqueous and lens. Müller and Buschke[2] have shown that in naphthaline cataracts, on injecting ascorbic acid intravenously, there was a regression of the opacities. Strauss[3] was of the opinion that in naphthaline cataracts the vitamin C disappears from the aqueous because of the increased permeability of the capsule. Bellows[4] recently has found a decrease in cevitamic acid content of blood plasma in patients with senile cataracts, as compared with

normal individuals. These cataractous subjects were also slower in responding to increased intake of vitamin C as shown by plasma determinations. Bellows concludes from these findings that the disappearance of vitamin C from the aqueous and lens in cataractous eyes precedes the lens changes, and is not secondary to them, as has been suggested. Fisher [5] has investigated the reducing substances, or auto-oxidation systems of the lens, and found that these are absent after formation of cataract. It may be that in cataracts associated with dinitrophenol there is some similar destruction of thes auto-oxidation systems. The work of Day, Langston, and Obrien,[6-10] on cataract formation in rats on vitamin G deficiency, brings up the problem of diet, and it has been thought that in this clinical group dietary insufficiency might play a part; but this seems unlikely, in view of the many cases of obesity under similar dietary restrictions without the administration of the drug. In view of the changes in the capsule, and immediately underneath the capsule, one might also think of a permeability change due to the dinitrophenol which might initiate a disturbance in the nutrition of the lens or an altered pH toward the acid side with the resultant lens opacities. It is difficult to explain the delayed formation of these cataracts after the use of dinitrophenol; in some cases more than a year elapsing from the time the drug was stopped to the onset of symptoms. Water balance or dehydration have been blamed as a possible mechanism, but this cannot be of sufficient degree to cause lens changes such as are found in Asiatic cholera. It is true that the marked increase in hyperopia noted early in many of these cases is suggestive of decreased lens volume with resultant change in refractive index of lens; but this may be due not to a change in volume of lens as much as a change in refractive index of individual fibers. These refractive changes are interesting in that they are the opposite of those in diabetic and traumatic cataracts.

In conclusion, the table as presented shows twenty eyes operated upon; but in the last two weeks three more patients with bilateral cataracts have appeared, and four more eyes than are shown in the table have been operated, all without complications. The results shown in the table, and in the additional cases just mentioned, justify a good prognosis as regards reëstablishment of useful vision to those afflicted with cataract formation coincident with ingestion of dinitrophenol and loss of weight resulting therefrom.

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DISCUSSION

M. N. Beigelman, M. D. (1930 Wilshire Boulevard, Los Angeles).—Although it was hardly more than a year ago that the coincidence of lenticular changes with dinitrophenol therapy became known, the "dinitrophenol cataract" today must be considered an established clinical entity. The general incidence of this complication, the appearance of the cataract, the rapidity of its development and other peculiarities in the course of the disease have been repeatedly investigated and reported. (See the article by Dr. Frank Rodin in the April issue of California and Western Medicine.)

The contribution of Dr. H. Barkan and of his collaborators deals with a less known but very important practical phase in the problem—the surgical treatment and the final results in this type of cataract.

It is fortunate indeed that the deleterious effect of dinitrophenol is limited to the crystalline lens without any other apparent intraocular change; this assures satisfactory visual results once the opaque lens is removed. The comparatively young age of these patients accounts for the favorable postoperative course: the rarity of postoperative inflammatory reactions and the speedy absorption of cortical material. Personally, I have resorted to the same extracapsular extraction that Doctor Barkan did. The lenticular intumescence which is responsible for a tautness of the capsule, in addition to the age of the patients, seemed to contraindicate the removal of the lens in toto. About the only difficulty encountered was an occasionally shallow anterior chamber; this made the use of a narrow Graefe knife preferable to a keratome section.

Doctor Barkan's experience, based on very large and carefully analyzed operative material, will be of decided value to anyone dealing with "dinitrophenol cataracts."

M. L. Tainter, M. D. (Stanford University School of Medicine, San Francisco).—Since this paper primarily deals with the results of cataract operations, I do not feel qualified to comment on the technical procedures described. However, the question of the etiology of these cataracts, just like that of most other cataracts, is still an unsolved problem. The sole fact relating these to dinitrophenol is that they have occurred in a number of women who, at some previous time, have taken this drug. Yet for every woman who has taken dinitrophenol and developed a cataract there are hundreds, if not thousands, who have taken equally large amounts and have not developed them. The limitation of the cataracts to women requires an explanation, since, while the drug has been administered to both sexes, yet men are apparently immune to any such change in the lens. Moreover, this type of cataract is not confined to those who have taken this drug, for several cases with a clinical picture, indistinguishable from that herein described, have occurred recently in women who have not taken dinitrophenol or any other reducing remedy. Dr. Warren D. Horner has a paper in press at the present time describing such cases. All these facts indicate that some other factor or factors must be operating to produce the

TABLE 1.—*Summary of Operative Cases and Postoperative Results*

Name	Sex	Age	Dinitrophenol	Vision Impaired	Vision Before Operation	Examination	Operation	Complications	Vision P. O.
I. W. Right eye	F.	31	May, 1934, to October, 1934, and February, 1935, to March, 1935. Maximum dose 480 mgs.	November 1, 1935	15/30—November 26, 1935 H. M. January 7, 1936	Intumescent silvery cataract a. c. very shallow, brownish post subcapsular opacities with many flakes.	January 7, 1936. Linear extraction, round pupil, no iridectomy, small cortical remnant.	None	15/20 with +10.0 sph.
I. W. Left eye	F.	31	Same	Same	15/30—November 26, 1935 Fingers 2 ft. January 7, 1936 H. M. January 10, 1936	Same	January 10, 1936. Linear extraction, round pupil, no iridectomy.	None	15/20 with +10.0 sph.
H. E. Right eye	F.	33	October, 1934-October, 1935, gr. 1½ daily, also thyroid.	October, 1935	15/15—October 10, 1935 15/100—December 20, 1935 following ascorbic acid for three weeks.	Cloth of gold opacity, many white punctate opacities in cortex, a. c. shallow.	Linear extraction, round pupil, flake of debris in pupil.	None	15/20 with +10.0 +2.0 c ×180
H. E. Left eye	F.	33	Same	Same	1/200 October 10, 1935	Intumescent silvery cataract, a. c. shallow, ascorbic acid three weeks prior to operation.	November 20, 1935. Linear extraction, round black pupil.	None	15/15 +12.0=+1.0 c x 135°
H. L. Right eye	F.	27	March to April, 1935 Amount?	September, 1935	H. M. December 9, 1935	Opalescent, intumescent cataract with sector-like opacities in anterior cortex, yellowish post-subcapsular opacity.	December 11, 1935. Linear extraction, some of the almost fluid lens escaped with incision, remainder easily expressed. Peripheral iridectomy.	None	20/20 +13.0=+1.0 c x 180°
H. L. Left eye	F.	27	Same	Same	15/70 December 9, 1935 H. M. December 15, 1935	Web-like yellowish post-subcapsular opacity. Punctate white opacities through anterior cortex most numerous under capsule, a. c. normal depth.	December 18, 1935. Linear extraction, some of the lens escaped with incision, remainder easily expressed. Peripheral iridectomy.	None	20/20 +13.0=+1.5 c x 180°
K. P. Right eye	F.	55	April, 1934, to October, 1934. Maximum dose three capsules daily.	September 1, 1935. Reading vision failed September 21, 1935.	H. M. 1 foot	Intumescent opalescent cataract, a. c. very shallow.	October 12, 1935, performed flap incision with Bard-Parker, enlarged with scissors. As capsule was opened soft lens material gushed out, nucleus expressed with spoons. Peripheral iridectomy.	None	15/20 +10=+1.50 c x 180° add +3.0
K. P. Left eye	F.	55	April, 1934, to October, 1934. Maximum dose three capsules daily.	September 1, 1935. Reading vision failed September 21, 1935.	H. M. 1 foot	Intumescent opalescent cataract, a. c. very shallow.	October 16, 1935, entrance to eye as above, capsulotomy, nucleus expressed and cortical debris removed with Hess spoon. Peripheral iridectomy.	Slight vitreous loss	15/15 Same correction as above
V. M. Right eye	F.	55	November, 1933, to June, 1935. 165 mgs.	Autumn, 1934	H. M. 1 foot	Silvery white, satiny, soft appearing, swollen cataract with broad white spoke-like striations from periphery to center.	Extraction with Weber loop after incision and iridectomy November 1, 1935.	Retrobulbar hemorrhage	10/200 +10.0 +2.0 ×180°

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TABLE 1.—*Summary of Operative Cases and Postoperative Results—(Continued)*

Name	Sex	Age	Dinitrophenol	Vision Impaired	Vision Before Operation	Examination	Operation	Complications	Vision P. O.
V. M. Left eye	F.	55	Same	Same	Same	Same	July 10, 1935. Combined extraction with complete iridectomy.	None	20/15 +12.0=+2.25× 180 add +3.0
C. R. Left eye			May, 1934, to May, 1935, one capsule daily, increased to two.	December, 1934. Rapid recent loss.	Fingers 4 feet R. and L.	Typical silvery sectors, intumescent shiny appearance.	December 31, 1935, combined extraction with iridectomy, complete. Large lens, capsule in coloboma.	Repeated small hemorrhage from wound, though a. c. restored.	To be refracted
R. H. Left eye	F.	45	March, 1934, to June, 1934, as many as q. i. d.	February, 1935	R — 1/10 LL. P. and P. Ascorbic acid	Capsular changes, cortical cloudy with sectors, post cortex cloth of gold.	Linear, large nucleus, scissors to enlarge incision, round pupil, no iridectomy.	None	20/15 +13.0=+0.5 c x 180°
R. H. Right eye	F.	45	Same	Same	Same	Same	February 18, 1936 Same as above	None	To be refracted
A. H. Right eye	F.	72	Amount ?	August, 1934	H. M. R. and L.	Intumescent dilated pupils a. c. shallow.	Difficult incision capsule thin and burse, complete iridectomy.	Diabetic secondary cataract.	20/20 +9.0=+4.0 c x× 180°
R. B. Right eye	F.	32	April, 1934, to October, 1934, 1 up to 6 capsules daily.	September, 1935	R. fingers 2 feet. L. 4/10, ascorbic with chills and fever.	Wide pupil, iris bulging forward, a. c. shallow. Anterior subcapsular opacities.	October 24, 1935, combined extraction, peripheral iridectomy, knife touched capsule, soft masses out quickly.	None	15/10 +13.0=+2.0 c x 5
R. B. Left eye	F.	32	Same	Same	Same	Same	February 5, 1936, linear extraction, round pupil, no iridectomy, no lenticular remains.	Postoperative iritis	20/20 +11.0 sph.
G. G. Left eye	F.	39	July, 1933, to September, 1933, and June to July, 1934. Total dose, 435 mgs.	May 23, 1935. Light projection	Light projection	Mature intumescent cataract flocculent mass of silvery lens materials, anterior capsule ruptured, shallow a. c.	June 12, 1935. Combined extraction, complete iridectomy.	Slight vitreous presentation	20/20 +10.00=+3.0× 180° add 3.5
E. S. Left eye	F.	56	July, 1934, one capsule t. i. d. Total 15 capsules only.	July, 1935	Fingers, at 1 foot	Mature, silvery, shiny, cataract, shallow chamber.	February 4, 1936, combined extraction, extracapsular large yellow nucleus, iridectomy, black pupil.	None	To be refracted
S. S. Right eye	F.	35	May 3, 1934, to November, 1935.	November, 1935	H. M. right eye 20/20 left eye	Mature, silvery, fluorescent posterior. Cloth of gold opacities. Sector-like opacities.	February 25, 1936, linear extraction with conjunctival flaps. No iridectomy.	None	To be refracted 20/20 O. D. 11.50S= +.37×15
E. B. Right eye	F.	28	June and July, 1934. Four capsules daily. July, 1935, for two weeks.	January 24, 1936	February 20, 1936, R. E. 3/200 L. E. 15/50. February 25, R. E. fingers, 1 foot, L. E. 15/100.	Silvery sector-shaped opacities. Shallow a. c. Many miniature white dots throughout cortex.	February 26, 1936 Linear extraction	None	To be refracted 20/20 +120=+1.25×30

clinical picture described by the present authors. There may be required the coincidence of a number of unrelated events in order to start these peculiar cataractous changes. However, dinitrophenol can scarcely be the essential factor when identical changes are seen in those who have never taken this drug.

Experimentally, dinitrophenol does not produce cataracts in animals on a normal diet, but it is quite easy to produce cataracts, without the addition of dinitrophenol, in animals on diets containing an excess of lactose (milk sugar), with low or rich content of vitamin G (Morgan and Cook: Proc. Soc. Exper. Biol. Med., 1936, 34:281); and there are many other unbalanced or modified diets reported to produce these experimental cataracts.

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W. D. HORNER, M. D. (384 Post Street, San Francisco).—In the *Journal of the American Medical Association* of July 13, 1935, together with Doctors Jones and Boardman, I published a description of three cases of bilateral cataract which followed the administration of dinitrophenol for obesity, and which we had studied for several months. In this report we emphasized the rapidity of the lenticular changes and the failure of any sort of treatment to retard the process. We strongly recommended that administration of dinitrophenol be stopped immediately pending further study. Our original descriptions of these cataracts and the assumed connection with dinitrophenol have been borne out since by more than a dozen published articles.

As has been stated, the treatment of these cataracts, as in most others, is surgical. Withdrawal of the drug, local and general measures have failed to influence progress.

Fortunately, no other ocular structure appears to be harmed in these cases, so that the prognosis is excellent if the lens be removed.

My personal surgical experience in these cases comprises seventeen extractions, fourteen of which were done by me and three more at which I assisted. Nearly all were private cases. It is remarkable that we have had only one patient report to the University of California Eye Clinic with this type of cataract.

We employed a narrow Graefe incision in some and a keratome in others. All were done with round pupils, using a peripheral iridotomy in the Graefe incisions and none at all in the linear extractions.

Visual results in the seventeen extractions were excellent. Fifteen, or eighty-two per cent, obtained final vision of 0.8 or better. A needling will be required in the remaining three cases. Our most serious complications were two cases of iritis. One healed with vision of 0.8, the other will require needling at some later date.

SPINAL ANESTHESIA AND THE ANESTHETIST*

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DISCUSSION *by Thomas O. Burger, M. D., San Diego; William W. Hutchinson, M. D., Los Angeles; Charles F. McCuskey, M. D., Los Angeles; Elmer M. Bingham, M. D., Riverside.*

MANY anesthetists have been more or less hostile to spinal anesthesia, partly because they have not developed a technique in which they could have confidence, and partly because its use has seemed to cut down the field of their work. This attitude among anesthetists has been engendered by the surgeons, many of whom have made a practice of administering the anesthetic themselves, then employing the referring doctor, an interne, or perhaps a convenient nurse, to look after the patient during the operation. As a result of this careless practice, the mortality incident on the use of spinal anesthesia has been too great, and this useful and valuable method has again been discredited.[1] However, when under the control of a competent and experienced anesthetist, with his knowledge of safety measures in connection with respiratory or circulatory failure, and with his gas-oxygen equipment at hand for instant use, spinal anesthesia becomes a relatively safe and satisfactory procedure. It seems, then, that every anesthetist should strive to perfect for himself a safe spinal anesthesia technique, so that when indicated he can wholeheartedly advocate its use. Briefly, then, we propose to outline such a technique.

PRELIMINARY EXAMINATION

First, is the preliminary visit to the patient, at which time his pulse and blood pressure should be checked and his general condition carefully appraised. This preoperative blood-pressure reading, taken before the ephedrin has been given, is absolutely essential if one is to correctly interpret the later changes to the best advantage. An effort should be made at this time to allay the fears of the patient, explaining something of the details of the anesthetic procedure if requested to do so, but by no means volunteering this information. The premedication which has been given should be noted; preferably, of course, it should have been arranged for previously in consultation with the surgeon. The use of a generous dose of one of the barbiturates is advisable, due to its protective action in the procain-sensitive individual. An average dose of one-sixth grain of morphin is indicated, but atropin should be omitted, since it tends to increase the heart rate, as does ephedrin. The usual dose of 50 milligrams of ephedrin should be ordered for administration, just as the patient enters the surgery. Contraindications to the use of spinal anesthesia, such as a history of coronary disease, advanced myocarditis, or the presence of any degree of shock, should be ruled out at this time. A pulse pressure of over 100, while not an absolute contraindication, should at least call for a reconsideration of the type of anesthetic to be used.

IMPORTANT FACTORS IN ADMINISTRATION OF ANESTHETIC

Regarding the administration of the anesthetic, we shall stress only the important points. First is position. Ordinarily it is best to make the injection with the patient lying on his side, his knees drawn well up on the abdomen, and his head bent downward as much as possible. One knee should be just over the other knee, the upper foot just over the under foot. The arms should be so disposed that the shoulders are as nearly as possible in a perpendicular line to the table. In case difficulty is encountered, it will often be found of great advantage to make the tap with the patient in the upright position. (Caution—Use no hypobaric solutions.) The method for doing this is to have the patient sitting on the side of the table, supported by an attendant, his feet resting on a stool, his back bent forward and downward as

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